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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/752,231	12/29/2000	Abraham Grossman	Q01/006	4570

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EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/752,231	<b>Applicant(s)</b> GROSSMAN, ABRAHAM	
	<b>Examiner</b> Jeanine A Goldberg	<b>Art Unit</b> 1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 October 2004.
- 2a) ☒ This action is **FINAL**.      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. This action is in response to the papers filed October 4, 2004. Currently, claims 1-13 are pending.
2. Any objections and rejections not reiterated below are hereby withdrawn in view of the amendments to the claims and the new grounds of rejection necessitated by amendment below.

### *Priority*

3. This application claims priority to PCT/US99/15030, filed July 1, 1999 and provisional application 60/091,578, filed July 2, 1998.

### *Drawings*

4. The drawings are objected to. Figure 1 contains a sequence which is not identified by SEQ ID NO: in either the brief description of the drawings or on the figure itself. Appropriate correction is required. The sequence appears as though it may be SEQ ID NO: 1.

**Response to amendments to the specification.** The Brief Description of Drawings is not found on page 7. The brief description of drawings is found on page 8. Appropriate correction is required prior to allowance.

The response filed October 4, 2004 states that an appropriate amendment has been made to include the sequence identity for Figure 1. This argument has been

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thoroughly reviewed, but is not found persuasive because the amendment appears to have been made to the wrong page and can not be entered.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Brown-2 et al. (Biochemistry, Vol. 34, pages 14765-14774, 1995) as evidenced by Chen et al. (Methods in Enzymology, Vol. 275, pages 503-520, 1996).

Brown et al. (herein referred to as Brown) teaches a method for identifying and characterizing two RNA binding sites on QB replicase. Brown-2 teaches using QB replicase, producing randomized RNA libraries and selecting RNAs. Specifically, Brown-2 teaches RNA from the mixed sequence population was used to initiate the QAB(+S1) selection and incubated with QB replicase and buffer. Those RNAs that bound the replicase were separated from the nonbound RNAs by filtering the binding reaction through a prewet nitrocellulose filter (page 14766, col. 1). The filter was then washed and the selected RNAs were removed from the filter and reverse transcribed, PCR amplified and transcribed using primers. Brown further teaches a QB (-30S) selection. The second selection was performed and nitrocellulose filtration was performed (page 14766, col. 2). Brown teaches that the selection was used to identify

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RNA ligands that bound with the highest affinity to QB replicase. Brown teaches that filter binding assays were done to determine the dissociation constants of these molecules for QB replicase. Brown-2 teaches that the minus strand of QB can be replicated in vitro by a replicase preparation lacking not only the host factor but ribosomal protein S1 as well. This observation suggests that an RNA binding site for minus strand recognition exists on one of the three remaining subunits (page 14765, col. 2). The elements of the target QB replicase are covalently bound to each other, thus, the target is covalently bonded to the catalytic entity.

Chen clearly teaches that nitrocellulose filtration preferentially retains RNA that is bound to proteins (i.e. a selection based upon affinity). Chen teaches that the method is used with much success and is both fast and convenient (page 507).

Thus, since Brown-2 teaches every limitation of the instant claims, Brown-2 anticipates the claimed invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (Methods in Enzymology, Vol. 275, pages 503-520, 1996).

Chen et al. (herein referred to as Chen) teaches a method for generating specific oligonucleotide inhibitors of viral polymerases. Chen specification teaches inhibitory templates by selection of RNA molecules replicated by QB replicase (page 512). Chen teaches that the newly synthesized minus strand and the original plus strand both serve as templates for complementary strand synthesis in a second round of replication. Chen teaches that a RNA repertoire is generated, and replicatable RNAs are selected.

Chen does not specifically teach in the analysis of QB performing an in vitro selection method to select oligonucleotides that bind to a target protein based on the affinity enrichment of the RNA pool. However, the beginning of the Chen articles teaches four general in vitro selection methods to select oligonucleotides that bind to a target protein based on the affinity enrichment of the RNA pool. The nitrocellulose filtration preferentially retains RNA that is bound to proteins. This methods has been used with much success and is both fast and convenient (page 507). Chen teaches using the nitrocellulose filtration to isolate high affinity oligonucleotides for four different RTs from RNA repertoires with  $10^{14}$  unique species. With nitrocellulose partitioning, the binding reaction is incubated and passed through the nitrocellulose filter and then the filter is washed to elute the RNAs recovered. Chen teaches that with nitrocellulose filtration in SELEX, background binding may be reduced by counter-selection and two different partitioning methods to eliminate the RNAs that are retained based on their ability to circumvent a single partitioning scheme (page 509). For the nitrocellulose filtration, only those RNA fragments that contain at least the minimum binding domain are bound by the protein and thus retained on nitrocellulose filters (page 510).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have analyzed QB replicase, much like the analysis of HIV-1RT, AMV-RT, M-MLV RT and FIV-RT analyzed in the first part of Chen. The ordinary artisan would have been motivated to have similarly studied QB, a replicase for ligand binding. During the analysis of QB, the ordinary artisan would have been motivated to have selected oligonucleotides that bind to a target protein based upon the affinity enrichment of the RNA pool. Chen teaches that nitrocellulose filtration preferentially retains RNA that is bound to proteins in a successful, fast and convenient manner (page 507). Thus, the ordinary artisan would have been motivated to have employed partitioning by nitrocellulose filtration to isolate high-affinity oligonucleotides for QB much like the analysis performed for the four different RTs taught by Chen.

### ***Conclusion***

7. **No claims allowable over the art.**

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

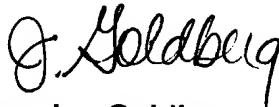
A) Gold et al. (US Pat. 5,270,163, December 1993) teaches a method for identifying nucleic acids ligands.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.



**Jeanine Goldberg**

**Patent Examiner**

December 23, 2004